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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/834,760

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Richard C. Austin

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20350 7590 02/19/2008  
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EXAMINER

ANGELL, JON E

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

02/19/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/834,760	AUSTIN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	J. E. Angell	1635	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 30 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 47-54 and 56-59 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 47-51, 53, 54 and 56-59 is/are rejected.
- 7) ☒ Claim(s) 52 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____.                                     |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____.   | 6) <input type="checkbox"/> Other: _____.                         |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/2007 has been entered.
2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 47-54 and 56-59 are currently pending and are examined herein.

### ***Drawings***

Applicants petition filed 10/30/2007 pursuant to 37 C.F.R. § 1.84(2) for colored drawings is acknowledged and has been approved.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1635

1. Claims 47-51, 53, 54 and 56-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method of inhibiting the generation of active thrombin on the surface of a cell within an atherosclerotic plaque within a mammal, said method comprising increasing the expression or activity of an ER resident calcium-binding protein in said cell by directly administering to said cell a polynucleotide operably linked to a promoter, wherein said polynucleotide encodes GRP78/BiP, whereby said GRP78/BiP is produced in said cell and the generation of active thrombin on the surface of said cell is inhibited,

does not reasonably provide enablement for the full scope encompassed by the claims.

Specifically, the specification does not provide an enabling disclosure for the claimed method wherein the ER resident calcium binding protein is a protein that is not GRP78/BiP. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the method commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

*Wands* states on page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

#### The nature of the invention and breadth of the claims

The instant claims are drawn to methods for inhibiting the generation of active thrombin on the surface of cells in a mammal by administering a nucleic acid encoding an ER resident calcium-binding protein to directly to said cell wherein the ER resident calcium-binding protein

is GRP78/BiP, GRP94, GRP72, Calreticulin, Calnexin, Reticulocalbin or Protein disulfide isomerase. Therefore the nature of the invention encompasses gene therapy.

The unpredictability of the art and the state of the prior art

Regarding the administration of a nucleic acid which encodes and expresses ER resident calcium binding proteins that are not GRP78/BiP, it is noted that the prior art does not teach that a ER resident calcium binding proteins are associated with the generation of active thrombin on the surface of cells. Therefore, without evidence indicating a sufficient number of ER resident calcium binding proteins can inhibit the generation of active thrombin on the surface of a cell, it is unpredictable that any ER resident calcium binding protein could inhibit the generation of active thrombin on the surface of a cell.

Working Examples and Guidance in the Specification

The specification discloses that expression of recombinant GRP78/BiP (an ER resident calcium binding proteins) inhibits the generation of active thrombin on the surface of cells (in vitro). There is no disclosure indicating that any ER resident calcium binding proteins other than GRP78/BiP is capable of inhibiting the generation of active thrombin on the surface of a cell. Considering that ER resident calcium binding proteins have different functions (such as Calcium regulation, protein folding, and protein transport) it is unpredictable which ER resident chaperone proteins could inhibit the generation of active thrombin on the surface of a cell.

#### Quantity of Experimentation

Considering the breadth of the claims, the unpredictable nature of the invention, and the limited guidance provided in the specification, additional experimentation would be required in order to practice the methods to the full scope encompassed by the claims. For instance, additional experimentation would have to be performed in order to determine if any of the ER resident calcium binding proteins other than GRP78/BiP could inhibit the generation of active thrombin. It is noted that in view of the fact that the art did not recognize an association between ER resident calcium binding proteins and thrombin generation, identification of any ER resident calcium binding protein as being associated with thrombin generation would be considered an advancement of the art. Therefore, the additional experimentation is not considered routine.

#### Level of the skill in the art

The level of the skill in the art is deemed to be high.

#### Conclusion

Considering the breadth of the claims, the unpredictable nature of the invention, the limited guidance provided in the specification and the high degree of skill required to practice the claimed methods, additional experimentation would be required in order to use the invention to the full scope encompassed by the claims. Based on the evaluation of all of the Wands factors, it is concluded that the amount of experimentation required to perform the broadly claimed invention is undue.

***Claim Objections***

2. Claim 52 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Response to Arguments***

3. Applicant's arguments filed 10/30/2007 have been fully considered and are persuasive in view of the amendment canceling claim 62. Therefore, the rejection has been obviated. However, upon further consideration, a new ground(s) of rejection is made for the reasons set forth herein.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/  
Primary Examiner, Art Unit 1635